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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/755,086	01/09/2004	David S. Lawrence	96700/860	8599

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EXAMINER	
PETERSEN, CLARK D	
ART UNIT	**PAPER NUMBER**
1657	

DATE MAILED: 12/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/755,086	LAWRENCE, DAVID S.	
	Examiner	Art Unit	
	Clark D. Petersen	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,49-123,127-131,133 and 134* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 January 2004* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1,3,4,70,79,80,82,84,85,92-94,96,101,110,111,113,115 and 120.

Continuation of Disposition of Claims: Claims rejected are 49-69,71-78,81,83,86-91,95,97-100,102-109,112,114,116-119,121-123,127-131,133 and 134.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group II, claims 49-123, 127-131, and 133-134, in the reply filed on 27 September 2006 is acknowledged.

Regarding species election, applicant's election for group A of isoforms α, β, and γ of protein kinase C, for group B of lipid, for group C of 7-nitrobenz-2-oxa-1,3-diazole, for group D of arylamine linker, and for group E of Compound 21 in Table 3 is acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1, 3, 4, 70, 79, 80, 82, 84, 85, 92-94, 96, 101, 110, 111, 113, 115, and 120 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group and nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 27 September 2006.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 49 and 88 are rejected under 35 U.S.C. 102(a) as being anticipated by Yeh et al (J Biol Chem, Papers in Press, 14 Jan 2002). The applied reference has a common author with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 102(a). This rejection under 35 U.S.C. 102(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Yeh et al teach a method for identifying an inhibitor of protein kinase C using a substrate described in the instant application. Yeh et al teach that the compound they

call compound 2, a ser-phe-arg-arg-arg-arg-lys peptide conjugated to an NBD moiety, can be phosphorylated by protein kinase C. Protein kinase C can be inhibited by adding PKC antibody to an assay mixture comprising compound 2, and measuring the resulting fluorescence of compound 2 (see Fluorescent PKC assay, p. 11528, col. 2, for example). Yeh et al also teach that one can add the PKC inhibitor staurosporine to a HeLa cell lysate comprising compound 2 and demonstrate a reduction in fluorescence intensity (see Additionally they teach that an assay using compound 2 can be performed in HeLa cells, in which compound 2 is microinjected into cells, and subsequently stimulated with TPA. The resulting fluorescence increase indicates active PKC within the cells (see Fig. 4, p. 11531, for example). Compound 2, described in Table 1, for example, is a substrate comprising a peptide and a fluorophore, and upon phosphorylation yields a 150% fluorescence increase. Therefore the teachings of Yeh et al are deemed to anticipate the instant claims 49 and 88.

Claims 49-69, 71-77, 81, 83, 86-88, 89, 90, 95, 97-100, 102-109, 112, 114, 116-119, 122, 123, 127-131, 133 and 134 are rejected under 35 U.S.C. 102(e) as being anticipated by Nguyen et al (US PGPub # 2004/0166553 A1).

Nguyen et al teach a photoactivatable protein kinase C sensor peptide, identical to that instantly claimed (see Fig. 59, for example). Nguyen et al also demonstrate the use of this sensor peptide in an assay characterizing a protein kinase C inhibitor (see p. 52, para [0543] to p. 53, [0549], for example; see Fig 59, for example). Nguyen et al teach that a caged kinase substrate can comprise fluorophores at either, or both ends,

of the peptide (see claims 18-28, for example). Nguyen et al also teach the substrate can comprise a lipid (see p. 3, para [0027], for example). The substrate can comprise a carrier (see p. 3, para [0027], for example). It is also possible to deliver caged sensors into living organisms, which inherently requires a pharmaceutically acceptable composition (see p. 39, para [0398], for example). Therefore the teachings of Nguyen et al are deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 50-61, 63-69, 72, 74, 81, 86, 89, 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yeh et al (J Biol Chem, 29 March 2002) in view of Haugland et al (US Patent # 5,635,608, issued 2 June 1997).

The teachings of Yeh et al are discussed above and applied as before.

Yeh et al do not expressly teach the addition of a photolabile caging moiety.

Haugland et al teach a photolabile caging moiety for protecting molecules. Haugland et al teach that photolysis of a caging group, i.e. by exposing a cell containing a caged molecule to light, makes it possible to release the parent compound into the biological system of interest with much better temporal and spatial resolution than it is

by simple diffusion of an uncaged molecule (see Background, col. 1, lines 22-28, for example). Haugland et al teach that one can attach a photolabile moiety of the structure recited in the instant application (see, e.g., claim 53) to a serine, threonine, or tyrosine, and that photolysis yields a normal serine, threonine, or tyrosine (see claim 10, col. 17, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to prepare caged, photoactivatable fluorescent kinase substrates as described in the instant application, because Haugland et al teaches that one can attach a photolabile moiety to a serine, threonine, or tyrosine, whereupon photoaction the serine, threonine, or tyrosine returns to its previous, biologically functional structure. Haugland teaches that this allows for better temporal and spatial resolution when observing cellular signaling phenomena.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to attach a photolabile caging moiety as recited in instant claim 53, for example, to fluorescent kinase substrates as taught by Yeh et al.

Claims 49-54, 56-58, 60, 61, 63-69, 72, 74, 78, 81, 83, 86, 89-91, 95, 97-100, 103, 105, 109, 112, 114, 116-119, 123, 127-131, 133, and 134 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chen et al (J Am Chem Soc, 12 Apr 2002, published on internet 22 Mar 2002) in view of Haugland et al (US Patent # 5,635,608, issued 2 June 1997).

The applied reference Chen et al has a common author with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art only under 35 U.S.C. 103(a). This rejection under 35 U.S.C. 103(a) might be overcome by: (1) a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not an invention "by another"; (2) a showing of a date of invention for the claimed subject matter of the application which corresponds to subject matter disclosed but not claimed in the reference, prior to the effective U.S. filing date of the reference under 37 CFR 1.131; or (3) an oath or declaration under 37 CFR 1.130 stating that the application and reference are currently owned by the same party and that the inventor named in the application is the prior inventor under 35 U.S.C. 104, together with a terminal disclaimer in accordance with 37 CFR 1.321(c). This rejection might also be overcome by showing that the reference is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(l)(1) and § 706.02(l)(2).

Chen et al teach a fluorescent reporter of kinase activity. Specifically, they teach a fluorescent reporter of kinase activity having the structure recited in claim 89 (see Scheme 1, p. 3841, for example). They teach that with the proper linker this substrate can demonstrate up to 250% increase in fluorescence when phosphorylated (see Table 1, p. 3841, for example). This substrate is specific for PKCα (see p. 3840, for example).

Chen et al do not expressly teach the use of a photolabile moiety to cage their fluorescent kinase reporter.

Haugland teaches a photolabile caging moiety. The teachings of Haugland are discussed above and applied as before.

A person of ordinary skill in the art at the time the invention was made would have been motivated to A person of ordinary skill in the art at the time the invention was made would have been motivated to prepare caged, photoactivatable fluorescent kinase substrates as described in the instant application, because Haugland et al teaches that one can attach a photolabile moiety to a serine, threonine, or tyrosine, whereupon photoaction the serine, threonine, or tyrosine returns to its previous, biologically functional structure. Haugland teaches that this allows for better temporal and spatial resolution when observing cellular signaling phenomena.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to attach a photolabile caging moiety as recited in instant claim 53, for example, to fluorescent kinase substrates as taught by Chen et al.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clark D. Petersen whose telephone number is (571)272-5358. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571)272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CDP
12/4/2006

JON WEBER
SUPERVISORY PATENT EXAMINER